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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/621,958	07/16/2003	Steven J. Locke	570002000100	2039

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EXAMINER	
VENCI, DAVID J	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 12/28/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/621,958	LOCKE ET AL.	
	Examiner	Art Unit	
	David J Venci	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *4-26-04*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-29* is/are pending in the application.

4a) Of the above claim(s) *28* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-27 and 29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-29* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-27 and 29, drawn to methods and preparations, classified in class 436/173, for example.

II. Claim 28, drawn to a kit, classified in class 435/975, for example.

The inventions are distinct, each from the other because of the following reasons:

The methods of Inventions I and the kit of Invention II are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case, the product as claimed can be used in a materially different process, such as an immunoassay.

The preparations of Inventions I and the kit of Invention II are independent and patentably distinct. Inventions are independent and patentably distinct if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case, the different inventions have different functions and modes of operation because the preparations of Invention I require a sample, while Invention II requires instructions.

Because these inventions are distinct for the reasons given above and the search required for Group I is not required for Group II, restriction for examination purposes as indicated is proper.

During a telephone conversation with Steve Todd, representative of Attorney Gerald Swiss, on December 6, 2004, a provisional election was made without traverse to prosecute the invention of Group I, claims 1-27 and 29. Affirmation of this election must be made by applicant in replying to this Office action. Claim 28 is withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Priority

Receipt is acknowledged of Canadian Application No. 2,393,726 submitted under 35 U.S.C. 119(a)-(d) on December 19, 2003, which papers have been placed of record in the file. The instant application repeats a substantial portion of the prior Canadian Application, and appears to add and claims additional disclosure not presented in the prior application, for example, Figs. 10-14. Since this application names an inventor or inventors named in the prior application, it may constitute a continuation-in-part of the prior application. Should applicant desire to obtain the benefit of the filing date of the prior application, attention is directed to 35 U.S.C. 120 and 37 CFR 1.78.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claim 27 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-27 and 29 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claims 1-3, 5, 15, 24-26 and 29, the recitation of "labelled" appears to be misspelled.

In claims 1, 24 and 26, the recitation of "differentially labelled" is indefinite because it is not clear how a set of isotopically labeled reagents are "differentially labelled" or whether differential labeling is due to differential isotope labeling.

In claims 1 and 24, the recitation of "a set" is indefinite because it is not clear what entities comprise or consist of "a set" or whether "a set" comprises multiple reagents of similar kind or multiple reagents of different kind.

In claims 1 and 3, the recitation of "the derivatized molecules in a preparation" lacks antecedent basis. In addition, the recitation of "a preparation" is indefinite because it is not clear what entities comprise or consist of "a preparation" or what steps or processes are required for "a preparation" or what physical parameters are required, if any, for "a preparation" state.

In claim 2, the recitation of "isotopically labelled in a preparation" is indefinite because the steps required for labeling "in a preparation" is not clear. In addition, the recitation of "a preparation" is indefinite because it is not clear what entities comprise or consist of "a preparation" or what steps or processes are required for "a preparation" or what physical parameters are required, if any, for "a preparation" state.

In claim 1, the recitation of "resulting in at least three differentially and isotopically labeled derivatives" is indefinite because it is stoichiometrically unclear how a reaction involving "two isotopically labelled

reagents" results in three isotopically labeled derivatives. In addition, it is not clear how a reaction results in three differentially labeled derivatives when it is not clear how a set of isotopically labeled reagents are "differentially labeled."

In claims 2-3, 25-26 and 29, the recitations of "the reductive alkylation" and "the amines" lack antecedent bases.

In claim 2, the recitation of "reacting the molecules, with isotopically labelled reagents" is indefinite because it is not clear whether "the molecules" are reacted with "isotopically labelled reagents" or whether "the molecules" comprise "isotopically labelled reagents."

In claims 4-5 and 8, the recitations of "prior to" and "before" are indefinite because it is not clear if/when the steps of "cleaving" or "denaturing" or "separating" occur in the method, or whether said steps are required claim limitations.

In claim 11, the recitation of "after" is indefinite because it is not clear when the step of "separating" occurs in the method.

In claim 14, the recitation of "the preparation of sequencing the molecule" lacks antecedent basis or is grammatically indefinite.

In claim 18, the recitation of "the sample" is indefinite because it is not clear which samples from claims 1 and 3 "the sample" is referencing.

In claim 20, the recitation of "the amines" lacks antecedent basis in claims 1 and 18-20.

In claims 24-26, the recitation of "A preparation" is indefinite because it is not clear what entities comprise or consist of "a preparation" or what steps or processes are required for "a preparation" or what physical parameters are required, if any, for "a preparation" state.

Claim 27 provides for the use of a mass spectrometer, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 2-6, 8-15, 17-23, 25-27 and 29 are rejected under 35 U.S.C. 102(e) as being anticipated by Aebersold et al. (US 6,670,194).

Aebersold et al. teach a method for the quantitative analysis (see Title, "Quantitative Analysis") of a sample of molecules (see col. 11, lines 35-39, "two or more protein samples", lines 47-54, "cell homogenates; cell fractions; biological fluids..." etc.) having an amine (see col. 10, lines 30-41, "PRGs... include... those that react with amino groups") bearing an active hydrogen comprising the steps of: reacting the molecules with isotopically labeled reagents (see Abstract, "affinity labeled protein reactive reagents") resulting in the reductive alkylation of the amines (see col. 10, lines 50-52, "amino reactive groups include aldehydes... in the presence... of $NaBH_4$ or $NaCNBH_4$") to their alkylamine derivatives,

such that the alkylamine derivatives are isotopically labeled (see Abstract, "The linker may be differentially isotopically labeled"), and examining the preparation by mass spectrometry (see Abstract, "reaction products are characterized by mass spectrometric (MS) techniques"). Examiner posits that Aebersold et al. explicitly teach a reaction of aldehydes (belonging to the PRGs) and amino groups (belonging to sample proteins) in the presence of $NaBH_4$ or $NaCNBH_4$. Consequently, the claimed "amine bearing an active hydrogen" and "alkylamine derivatives" necessarily result from this teaching of Aebersold et al. and would be so recognized by persons of ordinary skill in the art.

With respect to claims 3 and 29, Aebersold et al. teach a method for the quantitative analysis of two or more samples (see col. 11, lines 35-39, "two or more protein samples", lines 47-54, "cell homogenates; cell fractions; biological fluids..." etc.). In addition, Aebersold et al. teach the step of combining the derivatized molecules (see col. 6, lines 2-3, "The treated samples are then combined").

With respect to claims 4 and 29, Aebersold et al. teach a method comprising an additional step of cleaving the derivatized molecules prior to examining by mass spectrometry (see col. 6, lines 3-4).

With respect to claim 5, Aebersold et al. teach a method comprising an additional step of denaturing the molecules prior to reacting with isotopically labeled reagents (see col. 12, line 4-6).

With respect to claim 6, Aebersold et al. teach a method wherein electrospray ionization is used (see col. 11, lines 58-59).

With respect to claims 8-9, 11 and 29, Aebersold et al. teach a method comprising an additional step of separating derivatized molecules by 1D gel electrophoresis, 2D gel electrophoresis, or HPLC before examining by mass spectrometry (see col. 36, lines 11-12).

With respect to claim 10, Aebersold et al. teach a method comprising an additional step of separating the fragments after cleaving (see col. 19, lines 41-43).

With respect to claims 12-14 and 29, Aebersold et al. teach a method comprising an additional step of analyzing the preparation by CID in MS/MS mode to sequence the molecule (see col. 36, lines 19-36).

With respect to claims 15 and 17, Aebersold et al. teach a method wherein the isotopically labeled reagents are an aldehyde and a sodium borohydride reducing agent (see col. 10, lines 50-52).

With respect to claims 18-19 and 29, Aebersold et al. teach a method wherein the sample proteins are extracted from cells (see col. 5, line 63, "cell or tissue lysates").

With respect to claim 20, Aebersold et al. teach a method wherein the amines are lysine residues and N-terminal amino groups (see col. 18, lines 11-12).

With respect to claims 21-23, Aebersold et al. teach a method wherein an electrospray ionization ion trap spectrometer is used (see col. 22, lines 29-30).

With respect to claim 25, Aebersold et al. describe a preparation comprising

With respect to claims 25-26, Aebersold et al. describe a preparation comprising two or more samples (see col. 11, lines 35-39, "two or more protein samples", lines 47-54, "cell homogenates; cell fractions; biological fluids..." etc.), each sample comprising differentially and isotopically labeled derivatives (see Abstract, "The linker may be differentially isotopically labeled") resulting from the reductive alkylation of the amines (see col. 10, lines 50-52, "amino reactive groups include aldehydes... in the presence... of $NaBH_4$ or $NaCNBH_4$") to their alkylamine derivatives. The claimed "alkylamine derivatives" necessarily

results from the aforementioned teaching of Aebersold et al. and would be so recognized by persons of ordinary skill in the art.

With respect to claim 27, Aebersold et al. describe a method comprising a mass spectrometer (see Abstract).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 4-15, 17-27 and 29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Aebersold et al. (US 6,670,194) in view of Figeys et al. (US 2002/0076817).

Aebersold et al. teach a method for the simultaneous (see col. 11, line 40, "The samples are combined and processed as one") quantitative analysis (see Title, "Quantitative Analysis") of at least three samples (see col. 11, lines 35-39, "two or more protein samples", lines 47-54, "cell homogenates; cell fractions; biological fluids..." etc.) comprising the steps of: reacting each sample with a set of isotopically labeled reagents (see Abstract, "affinity labeled protein reactive reagents") wherein the set of isotopically labeled reagents is differentially labeled (see Abstract, "The linker may be differentially isotopically labeled"), combining the derivatized molecules in a preparation (see col. 6, lines 2-3, "The treated samples are then combined"), and examining the preparation by mass spectrometry (see Abstract, "reaction products are characterized by mass spectrometric (MS) techniques").

Aebersold et al. do not teach the step of using "at least two" isotopically labeled reagents, resulting in "at least three" derivatives.

However, Figeys et al. teach the step of using two isotopically labeled reagents (see Fig. 6, "O^{16}-water" and "O^{18}-water") resulting in three derivatives (see Fig. 6, "Peptides mixture") in order to label individual samples with distinct isotope ratios (see para. [0010]). Therefore, it would have been obvious for a person of ordinary skill in the art to modify the simultaneous quantitative method of Aebersold et al. with the use of two isotopically labeled reagents because Figeys et al. teach that labeling individual samples with distinct isotope ratios allows a convenient means for "sample tracking" which allows a peptide to be traced back to its sample source (see para. [0036]).

With respect to the limitations of claims 4-6, 8-15, 17-23, 25-27 and 29, please see rejection under 35 U.S.C. 102(e) in view of Aebersold et al. (US 6,670,194) set forth supra.

With respect to claim 7, Figeys et al. teach a method wherein ionspray is used (see para. [0055]).

With respect to claim 24, Figeys et al. describe a preparation using two isotopically labeled reagents (see Fig. 6, "O^{16}-water" and "O^{18}-water").

Claim 16 is rejected under 35 U.S.C. 103(a) as being unpatentable over Aebersold et al. (US 6,670,194) and Figeys et al. (US 2002/0076817) as applied to claims 1 and 15, and further in view of Vandekerckhove & Gevaert (US 2004/0005633).

Aebersold et al. and Figeys et al. teach a method for the simultaneous quantitative analysis of at least three samples as substantially described supra. The aforementioned references do not teach a method wherein formaldehyde and acetaldehyde are used.

However, Vandekerckhove & Gevaert teach the use of deuterated formaldehyde and acetaldehyde (see para. [0107]) in order to induce a distinguishable mass shift in peptide analysis. Therefore, it would have been obvious for a person of ordinary skill in the art to modify the method of Aebersold et al. and Figeys et al. with the use of formaldehyde and acetaldehyde because Vandekerckhove & Gevaert teach that induction of distinguishable mass shifts, e.g. with deuterated formaldehyde or acetaldehyde, allows isolation and identification of peptides in complex mixtures (see para. [0002] to [0004]).

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J Venci whose telephone number is 571-272-2879. The examiner can normally be reached on 08:00 - 16:30 (EST). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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